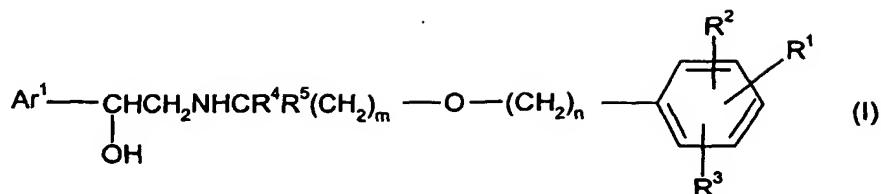


## CLAIMS

## 1. A compound of formula (I)

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or a salt, solvate, or physiologically functional derivative thereof, wherein:

10 m is an integer of from 2 to 8;

n is an integer of from 3 to 11, preferably from 3 to 7;

with the proviso that m + n is 5 to 19, preferably from 5 to 12;

15 R¹ is -XNR⁶C(O)NR⁷R⁸; wherein

X is selected from -(CH<sub>2</sub>)<sub>p</sub>- and C<sub>2-6</sub>alkenylene;

R<sup>6</sup> and R<sup>8</sup> are independently selected from hydrogen, C<sub>1-6</sub>alkyl and C<sub>3-7</sub> cycloalkyl; wherein

20 said C<sub>1-6</sub>alkyl and C<sub>3-7</sub> cycloalkyl moieties may optionally be substituted by -CO<sub>2</sub>H or -CO<sub>2</sub>(C<sub>1-4</sub>)alkyl;

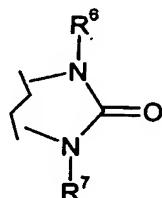
25 R<sup>7</sup> is selected from hydrogen, C<sub>1-6</sub>alkyl, C<sub>3-7</sub>cycloalkyl, -C(O)R<sup>9</sup>, phenyl, naphthyl, hetaryl, and phenyl(C<sub>1-4</sub>alkyl)- and R<sup>7</sup> is optionally substituted by 1 or 2 groups independently selected from halo, hydroxy, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, C<sub>1-6</sub> alkoxy, -NHC(O)(C<sub>1-6</sub>alkyl), -SO<sub>2</sub>(C<sub>1-6</sub>alkyl), -SO<sub>2</sub>(phenyl), -CO<sub>2</sub>H, and -CO<sub>2</sub>(C<sub>1-4</sub>alkyl) and CONR<sup>10</sup>R<sup>11</sup>;

30 R<sup>9</sup> is selected from C<sub>1-6</sub>alkyl, C<sub>3-7</sub>cycloalkyl, -CO<sub>2</sub>H, CO<sub>2</sub>(C<sub>1-4</sub>alkyl), phenyl, naphthyl, hetaryl, and phenyl(C<sub>1-4</sub>alkyl)- and R<sup>9</sup> is optionally substituted by 1 or 2 groups independently selected from halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, C<sub>1-6</sub> alkoxy, -NHC(O)(C<sub>1-6</sub>alkyl), -SO<sub>2</sub>(C<sub>1-6</sub>alkyl), -SO<sub>2</sub>(phenyl), -CO<sub>2</sub>H, and -CO<sub>2</sub>(C<sub>1-4</sub>alkyl);

$R^{10}$  and  $R^{11}$  each independently represent hydrogen,  $C_{1-4}$ alkyl or  $C_{3-7}$  cycloalkyl, and

5  $p$  is an integer from 0 to 6, preferably from 0 to 4;

or  $R^1$  is cyclised such that  $R^8$  forms a bond with the phenyl ring to which  $R^1$  is attached, via the ring carbon atom adjacent to  $R^1$ , so as to form a moiety of the formula:



10

$R^2$  is selected from hydrogen,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy, phenyl, halo, and  $C_{1-6}$ haloalkyl;

$R^3$  is selected from hydrogen, hydroxy,  $C_{1-6}$ alkyl, halo,  $C_{1-6}$ alkoxy, phenyl,  $C_{1-6}$ haloalkyl, and  $-\text{SO}_2\text{NR}^{12}\text{R}^{13}$ ;

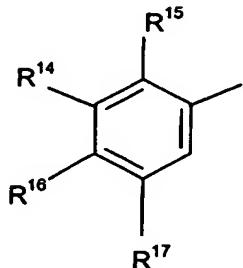
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wherein  $R^{12}$  and  $R^{13}$  are independently selected from hydrogen,  $C_{1-6}$ alkyl,  $C_{3-6}$ cycloalkyl, phenyl, and phenyl ( $C_{1-4}$ alkyl), or  $R^{12}$  and  $R^{13}$ , together with the nitrogen to which they are bonded, form a 5-, 6-, or 7- membered nitrogen containing ring; and  $R^{12}$  and  $R^{13}$  are each optionally substituted by one or two groups selected from halo,  $C_{1-6}$ alkyl, and  $C_{1-6}$ haloalkyl;

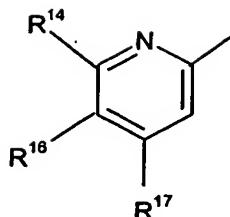
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$R^4$  and  $R^5$  are independently selected from hydrogen and  $C_{1-4}$ alkyl with the proviso that the total number of carbon atoms in  $R^4$  and  $R^5$  is not more than 4;

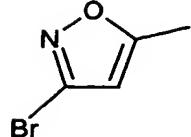
and Ar<sup>1</sup> is a group selected from



(a)

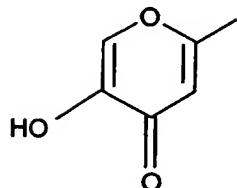


(b)



(c)

and



(d)

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wherein R<sup>14</sup> represents hydrogen, halogen, -(CH<sub>2</sub>)<sub>q</sub>OR<sup>18</sup>, -NR<sup>18</sup>C(O)R<sup>19</sup>, -NR<sup>18</sup>SO<sub>2</sub>R<sup>19</sup>, -SO<sub>2</sub>NR<sup>18</sup>R<sup>19</sup>, -NR<sup>18</sup>R<sup>19</sup>, -OC(O)R<sup>20</sup> or OC(O)NR<sup>18</sup>R<sup>19</sup>, and R<sup>15</sup> represents hydrogen, halogen or C<sub>1-4</sub> alkyl;

10 or R<sup>14</sup> represents -NHR<sup>21</sup> and R<sup>15</sup> and -NHR<sup>21</sup> together form a 5- or 6- membered heterocyclic ring;

R<sup>16</sup> represents hydrogen, halogen, -OR<sup>18</sup> or -NR<sup>18</sup>R<sup>19</sup>;

15 R<sup>17</sup> represents hydrogen, halogen, haloC<sub>1-4</sub> alkyl, -OR<sup>18</sup>, -NR<sup>18</sup>R<sup>19</sup>, -OC(O)R<sup>20</sup> or OC(O)NR<sup>18</sup>R<sup>19</sup>;

R<sup>18</sup> and R<sup>19</sup> each independently represents hydrogen or C<sub>1-4</sub> alkyl, or in the groups

$-\text{NR}^{18}\text{R}^{19}$ ,  $-\text{SO}_2\text{NR}^{18}\text{R}^{19}$  and  $-\text{OC(O)NR}^{18}\text{R}^{19}$ ,  $\text{R}^{18}$  and  $\text{R}^{19}$  independently represent hydrogen or  $\text{C}_{1-4}$  alkyl or together with the nitrogen atom to which they are attached form a 5-, 6- or 7- membered nitrogen-containing ring,

5  $\text{R}^{20}$  represents an aryl (eg phenyl or naphthyl) group which may be unsubstituted or substituted by one or more substituents selected from halogen,  $\text{C}_{1-4}$  alkyl, hydroxy,  $\text{C}_{1-4}$  alkoxy or halo  $\text{C}_{1-4}$  alkyl; and

q is zero or an integer from 1 to 4;

10

provided that in the group (a) when  $\text{R}^{14}$  represents  $-(\text{CH}_2)_q\text{OR}^{18}$  and q is 1,  $\text{R}^{16}$  is not OH.

2. A compound of formula (I) as defined in claim 1 wherein  $\text{R}^6$  and  $\text{R}^8$  are independently selected from hydrogen,  $\text{C}_{1-6}$ alkyl and  $\text{C}_{3-7}$  cycloalkyl;

15  $\text{R}^7$  is selected from hydrogen,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{3-7}$ cycloalkyl,  $-\text{C(O)R}^9$ , phenyl, naphthyl, hetaryl, and phenyl( $\text{C}_{1-4}$ alkyl)- and  $\text{R}^7$  is optionally substituted by 1 or 2 groups independently selected from halo, hydroxy,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{1-6}$ haloalkyl,  $\text{C}_{1-6}$  alkoxy,  $-\text{NHC(O)(C}_{1-6}\text{alkyl)}$ ,  $-\text{SO}_2(\text{C}_{1-6}\text{alkyl})$ ,  $-\text{SO}_2(\text{phenyl})$ ,  $-\text{CO}_2\text{H}$ , and  $-\text{CO}_2(\text{C}_{1-4}\text{alkyl})$ ;

$\text{R}^{14}$  is as defined above except that  $\text{R}^{14}$  does not represent hydrogen; and

20 all other substituents are as defined for formula (I).

or a salt, solvate or physiologically functional derivative thereof.

3. A compound according to claim 1 or claim 2 wherein  $\text{R}^{14}$  represents hydrogen,

25 halogen,  $-\text{NR}^{18}\text{C(O)R}^{19}$ ,  $-\text{NR}^{18}\text{SO}_2\text{R}^{19}$ ,  $-\text{SO}_2\text{NR}^{18}\text{R}^{19}$ ,  $-\text{NR}^{18}\text{R}^{19}$ ,  $-\text{OC(O)R}^{20}$  or  $\text{OC(O)NR}^{18}\text{R}^{19}$ ; and  $\text{R}^{16}$  represents hydrogen, halogen,  $-\text{OR}^{18}$  or  $-\text{NR}^{18}\text{R}^{19}$ .

4. A compound according to claim 1 or claim 2 wherein  $\text{R}^{14}$  represents hydrogen,

halogen,  $-(\text{CH}_2)_q\text{OR}^{18}$ ,  $-\text{NR}^{18}\text{C(O)R}^{19}$ ,  $-\text{NR}^{18}\text{SO}_2\text{R}^{19}$ ,  $-\text{SO}_2\text{NR}^{18}\text{R}^{19}$ ,  $-\text{NR}^{18}\text{R}^{19}$ ,  $-\text{OC(O)R}^{20}$  or  $\text{OC(O)NR}^{18}\text{R}^{19}$ ; and  $\text{R}^{16}$  represents hydrogen, halogen, or  $-\text{NR}^{18}\text{R}^{19}$ .

5. A compound of formula (I) according to any of claims 1 to 4 wherein  $\text{R}^1$  represents  $-(\text{CH}_2)_p\text{NHC(O)NHR}^7$ .

35 6. A compound according to any of claims 1 to 5 wherein p is 0, 1 or 2.

7. A compound of formula (I) which is selected from:

*N*-[3-(4-[(2*R*)-2-[3-(Formylamino)-4-hydroxyphenyl]-2-hydroxyethyl]amino)hexyl]oxy]butyl]phenyl]urea;

*N*-[3-(4-[(6-((2*R*)-2-[3-(Formylamino)-4-hydroxyphenyl]-2-

5 hydroxyethyl]amino)hexyl]oxy]butyl]phenyl]-*N*-phenylurea;

*N*-[3-(4-[(6-((2*R*)-2-[3-(Formylamino)-4-hydroxyphenyl]-2-

hydroxyethyl]amino)hexyl]oxy]butyl]phenyl]-*N*-pyridin-3-ylurea;

*N*-[3-(4-[(6-(2-hydroxy-2-[5-hydroxy-6-(hydroxymethyl)pyridin-2-

30 yl]ethyl]amino)hexyl]oxy]butyl]-5-methylphenyl]urea.

and salts, solvates, and physiologically functional derivatives thereof.

8. A method for the prophylaxis or treatment of a clinical condition in a mammal, such as a human, for which a selective  $\beta_2$ -adrenoreceptor agonist is indicated, which comprises

15 administration of a therapeutically effective amount of a compound of formula (I), (Ia) or (Ib) according to any of claims 1 to 7, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof.

9. A compound of formula (I) according to any of claims 1 to 7 or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof for use in medical therapy.

10. A pharmaceutical formulation comprising a compound of formula (I) according to any of claims 1 to 7 or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof, and a pharmaceutically acceptable carrier or excipient, and optionally one or more other therapeutic ingredients.

11. A combination comprising a compound of formula (I) according to any of claims 1 to 7 or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof, and one or more other therapeutic ingredients.

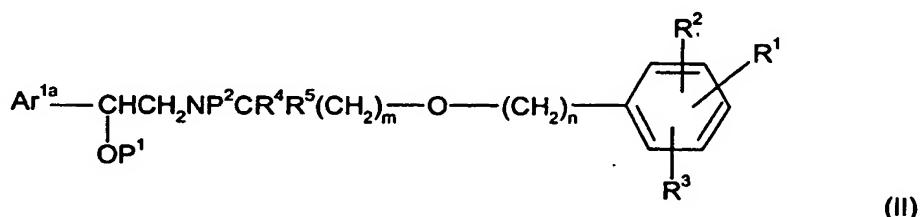
12. A combination according to claim 11 wherein the other therapeutic ingredient is a corticosteroid, an anticholinergic or a PDE4 inhibitor.

35 13. The use of a compound of formula (I) according to any of claims 1 to 7, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof

in the manufacture of a medicament for the prophylaxis or treatment of a clinical condition for which a selective  $\beta_2$ -adrenoreceptor agonist is indicated.

14. A process for the preparation of a compound of formula (I) according to any of  
5 claims 1 to 7, or a salt, solvate, or physiologically functional derivative thereof, which  
comprises:

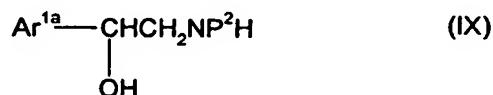
(a) deprotection of a protected intermediate, for example of formula (II):



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or a salt or solvate thereof, wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $m$ , and  $n$  are as defined for the compound of formula (I),  $Ar^{1a}$  represents an optionally protected form of  $Ar^1$ ; and  $P^1$  and  $P^2$  are each independently either hydrogen or a protecting group, provided that the compound of formula (II) contains at least one protecting group.

**(b) alkylation of an amine of formula (IX)**

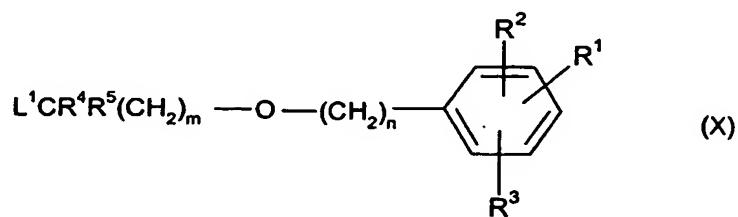


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wherein  $\text{Ar}^{1a}$  is an optionally protected form of  $\text{Ar}^1$  and  $\text{P}^2$  is either hydrogen or a protecting group.

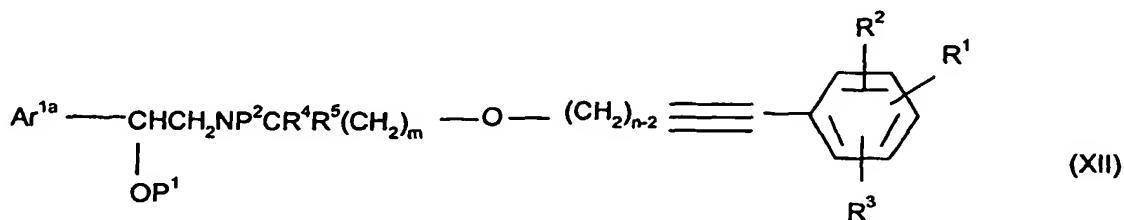
with a compound of formula (X):

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wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $m$ , and  $n$  are as defined for the compound of formula (I) or (Ia) and  $L^1$  is a leaving group;

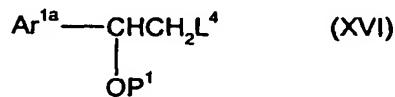
5 (c) reduction of a compound of formula (XII):



wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $m$  and  $n$  are as defined for formula (I),  $\text{Ar}^{1a}$  is an optionally protected form of  $\text{Ar}^1$ , and  $P^1$  and  $P^2$  are each independently hydrogen or a protecting group as defined above;

10

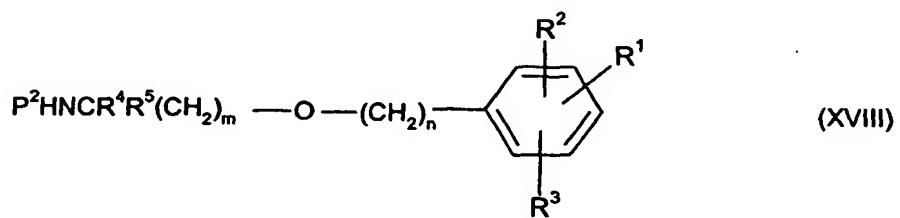
(d) reacting a compound of formula (XVI):



wherein  $\text{Ar}^{1a}$  is an optionally protected form of  $\text{Ar}^1$ , and  $P^1$  is hydrogen or a protecting group and  $L^4$  is a leaving group as defined above for groups  $L-L^3$  or a compound of formula (XVII):



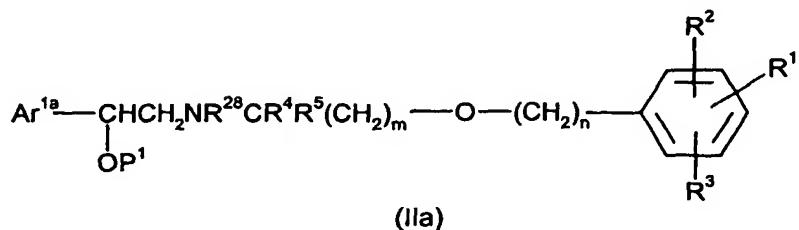
wherein  $\text{Ar}^{1a}$  is as hereinbefore defined with an amine of formula (XVIII):



wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $P^2$ ,  $m$  and  $n$  are as defined for formula (II); or

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(e) removal of a chiral auxiliary from a compound of formula (IIa):



wherein  $R^1$  ~  $R^5$ ,  $m$  and  $n$  are as defined for formula (I),  $Ar^{1a}$  and  $P^1$  are as defined for formula (II) each independently represent hydrogen or a protecting group and  $R^{28}$  represents a chiral auxiliary.

followed by the following steps in any order:

- (i) optional removal of any protecting groups;
- 15 (ii) optional separation of an enantiomer from a mixture of enantiomers;
- (iii) optional conversion of the product to a corresponding salt, solvate, or physiologically functional derivative thereof.